UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,072	07/03/2003	David Lewis	239775US0DIV	3477

22850 7590 04/19/2006

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,072	LEWIS ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/20/06 has been entered.

Receipt is also acknowledged of the amendments and remarks filed on 11/21/05. Claims 33-49 have been added while no claims have been cancelled. Claims 11, 16, 19, 21, 26 and 28 have been amended. Accordingly claims 11-49 are pending.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 11, 14-23, 26-30, 33-34, 39-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cutie (6,129,905) in view of Tzou et al (5,776,433).

Cutie teaches aerosol formulations for mucosal and/or topical administration containing one or more drugs and a sugar as a dispersant in a pharmaceutically acceptable propellant. Metered dose inhalers suitable for delivering such formulations are also disclosed. Cutie discloses that in an aerosol drug formulation the drug may be dissolved in the propellant (col. 1, lines 24-29). In a solution formulation, a cosolvent

may be added to enhance drug dissolution (col. 2, lines 3-10). The formulations may contain ethanol up to 5% of the formulation (col. 5, lines 5-9). Drugs which may be administered via the said formulations include flunisolide, beclomethasone, triamcinolone, budesonide (col. 4, lines 25-35). The said formulations may contain excipients such as antioxidants (col. 5, lines 31-34). The formulations may be filled into conventional aerosol containers using conventional filling equipment well known to those skilled in the art (col. 5, lines 40-45). Examples such as example 5, 7, 8 and 11 show formulations comprising an active agent such as triamcinolone or flunisolide, ethanol and propellant. Cutie lacks disclosure on specific antioxidants such as butylated hydroxyanisole and the canister specifics.

Tzou teaches flunisolide aerosol formulations comprising a therapeutically effective amount of flunisolide in solution with ethanol and a propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane and a mixture thereof used for the treatment of bronchial asthma. The formulations may be delivered by a metered dose inhaler with a canister that is inert to flunisolide (see abstract). Tzou discloses that NASALIDE® nasal solution comprises excipients such as butylated hydroxyanisole (col. 1, lines 17-26). It is also disclosed that in the formulations of the invention, the flunisolide is fully dissolved and the formulation is free from undissolved flunisolide (col. 2, lines 36-40). Aerosol canisters equipped with conventional valves, preferably metered dose valves (col. 3, lines 45-50). Conventional aerosol canisters can be used to contain a formulation of the invention. The

formulations are contained within a glass aerosol vial or an aluminum aerosol vial having an interior formulation chamber coated with a resin that is inert to flunisolide and preferably does not absorb flunisolide from the formulation. Suitable resins for coating the formulation chamber include materials commonly employed as interior can coatings, such as epoxy resins (e.g. epoxy-phenolic resins and epoxy-urea formaldehyde resins).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general formulations of Cutie on solution formulations of corticosteroids for inhalation and treatment of respiratory disorders to have looked in the art for specific antioxidants and specific aerosol canisters that would improve stability and efficiency of the inhaled formulations as taught by Tzou.

Claims 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cutie (6,129,905) in view of Tzou et al (5,776,433) as applied to claims 11, 14-23, 26-30, 33-34, 39-49 above, and further in view of Riebe et al (6,558,651).

Cutie and Tzou, discussed above, lack specific disclosure on the inner surface of the metered dose being composed of anodized aluminum or stainless steel.

Riebe et al teaches aerosol formulations and the suitable canisters for metered dose inhalers. The formulations may be filled into canisters capable of withstanding the vapor pressure of the propellant, such as plastic, plastic-coated glass bottle or preferably a metal can, for example an **aluminum can which may be anodized**,

lacquer-coated and/or plastic coated, which container is closed with a metering valve. The MDI can may be a coated metal can such as **aluminum or stainless steel** (see col. 5, lines 20-55).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general formulations of the combined references of Cutie and Tzou on solution formulations of corticosteroids for inhalation and treatment of respiratory disorders filled into conventional metered dose inhalers to have looked in the art for specific aerosol canisters that would improve stability and efficiency of the inhaled formulations as taught by Riebe et al.

Claims 11, 14-19, 21-23, 26, 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rovee et al (4,185,100) in view of Cutie (5,891,419).

Rovee teaches a pharmaceutical composition for topical treatment of skin disorders comprising an anti-inflammatory corticosteroid. The suitable corticosteroids include triamcinolone acetonide (col. 2, lines 62-68). The solvents include ethanol and propylene glycol (col. 3, lines 25-26 and tables A and F). The suitable anti-oxidants include butylated hydroxytoluene (col. 4, lines 41-44; col. 5, lines 45-47). Table F discloses propellant for aerosol formulations. Rovee lacks specific disclosure on HFA propellants.

Cutie teaches aerosol formulations for oral inhalation containing flunisolide dispersed in HFC 134a and/or HFC 227, and metered dose inhalers suitable for

delivering such formulations. Said formulations contain small amounts of ethanol. Cutie teaches that ethanol may be included in an amount effective to wet and aid in dispersing the flunisolide in the formulation, without dissolving the flunisolide in the formulation (col. 3, lines 39-42). The formulations also contain antioxidants (col. 4, line 43). Cutie discloses that said formulations are suitable for treating respiratory disorders such as bronchial asthma (col. 3, lines 43-45).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general formulations of Rovee et al to have looked in the art for specific propellants which are better suited for environments and patients, as taught by Cutie et al, with a reasonable expectations of successfully preparing safe and effective aerosol preparations. It is well known in the art, as shown by Cutie and others that over the past decade or so CFC propellants have been replaced by HFA propellants, and thus use of HFA propellants is not a support for patentability.

Claims 11, 15-23, are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al (WO 9834595).

Keller teaches medical aerosol formulations which comprise an active agent, a propellant mixture, a cosolvent and other optional additives. The suitable active agents include budesonide available in an amount of from 0.001 to 5% by weight (page 16, line 2 and page 17, line 30 to page 18, line 2). The preferred cosolvents, which are particularly advantageous in the solution formulations, include ethanol and propylene

glycol which are generally available in an amount of 0.1 to 30% by weight (page 19, lines 11-28 and claims). The propellants include HFA 134a and HFA 227, generally available in an amount of at least 64% (claim11). Keller discloses use of vitamin E in the formulation (as an active agent).

Keller also discloses that the active agent can be used in a pharmaceutically acceptable salt form (page 17, lines 26-29).

Although Keller does not disclose use of vitamin E as an antioxidant, Keller discloses their use in the formulation. Vitamin E is a known antioxidant and thus preparing such formulations would have been a logical extension of the teachings of Keller, and that said modifications would have been obvious to one of ordinary skill in the art.

Claims 12-15, 20, 24-25, 27, 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cutie (6,129,905) in view of Tzou et al (5,776,433) and further in view of Radhakrishnan et al (5,192,528).

Cutie, discussed above, lacks disclosure on specific antioxidants and budesonide.

Radhakrishnan teaches corticosteroid inhalation treatment methods of delivering a therapeutic dosage of corticosteroid drug to the lungs. The corticosteroids include flunisolide, budesonide, etc (col. 4, lines 14-25). The formulation (described in example

1) is formed by adding alpha-tocopherol with the corticosteroid and lipids (col. 4, lines 34-37).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general formulations of Cutie for inhalation administration of corticosteroids and antioxidants, to have looked in the art for more specific antioxidants suitable for combination with corticosteroids for inhalation, as taught by Radhakrishnan, with reasonable expectations of successfully preparing stable and effective formulations. Furthermore it would have been obvious to a person of ordinary skill in the art to have chosen other corticosteroids such as budesonide or other antioxidants such as ascorbyl palmitate.

Double Patenting

The provisional rejection of claims 11-32 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/244,519 is maintained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed on 11/21/05 have been fully considered but they are not persuasive.

Applicant argues that Rovee et al does not teach the claimed compositions because Rovee does not teach antioxidants in the formulations as claimed and does not specifically teach the HFA propellants. This is not persuasive because the claims are drawn to a formulation comprising a corticosteroid, an antioxidant and a propellant/cosolvent vehicle. Rovee teaches the antioxidants in an aqueous/alcoholic solution, as mentioned by the applicant (see Remarks page 10, lines 15-16). Also disclosed are the solutions of corticosteroids. Aerosol formulations are taught, without mention of HFA propellants. However, as shown by Cutie addition of HFA propellants is well known and widely practiced in the art. Thus a combination of Rovee and Cutie meets all the limitations of the said claims.

Applicant argues that Keller et al is disclosing a fluorinated alkane propellant and carbon dioxide. Applicant is referring to Examples 4 and 5 which disclose a steroid in the presence of an HFA/CO2 propellant. This is not commensurate with the scope of the claims. Instant claims are formulation claims which use the open language of "comprising". Use of CO2 in the instant formulations is not excluded. It is also noted that the amount of CO2 in Keller's formulations is very very small (0.001%). It is almost impossible to determine that the claimed formulations do not contain 0.001% CO2. Thus it is considered that Keller reference is meeting all the limitations of the rejected claims.

Applicant argues that in Cutie's reference ethanol is "to prevent dissolution" of the flunisolide. Applicant further states that "this disclosure is directly at odds with the present invention wherein a cosolvent (e.g. ethanol) is used to dissolve the active ingredient in the propellant". Although the statement is correct, the argument is not

persuasive. Cutie teaches that ethanol should be added at a level not to dissolve flunisolide in the formulation. This is clearly teaching one of ordinary skill in the art that if more ethanol is used flunisolide is dissolved and that the resulting formulation is a "solution".

Applicant argues that Radhakrishnan et al does not compensate for the deficiencies of Cutie. This is not persuasive because as stated in the rejection, Cutie lacks specific disclosure on the use of specific antioxidants, and Radhakrishnan teaches the specific antioxidants in similar formulations. The fact that Radhakrishnan is teaching suspensions does not teach away from addition of specific antioxidants. It is noted that Cutie discloses addition of antioxidants. Radhakrishnan was used as a support to teach specific antioxidants known in the art.

With regard to the double patenting rejection over the copending application, U.S. 10/244,519, Applicant argues that if the co pending application is not yet in condition for allowance, the said rejection should be with drawn. Applicant is correct and the provisional double patenting rejection in (the two co-pending applications) the application placed in condition for allowance first, will be withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L. Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mina Haghighatian
April 13, 2006

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER